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/(54) DIPHENYI, AZETIDINONE DERIVATIVES POSSESSING CHOLESTEROL ARSORPTION INDIBLYORY ACTIVITY

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	C97D 483/82	(2006.01)

514/210.02; 514/414; 514/422; U.S. Cl. 548/465; 548/518; 548/95Z ABSTRACT

(57)

Compounds of formula (i) (wherein variable groups are as defined within) pharmacentically screptable salts, solvates, solvates of such saits and prodrigs thereof and their use as cholesterol absorption inhibitors for the treatment of hyper-lipidscands are described. Processes for their manufacture and phermacentical compositions containing them are also described

Mar. 13, 2008

-continued		
Compound (I)	Caeo Valua (10° cm/sec)	
H-{[4-((3%,5%)-1-(4-fluorophenyi)-3-([2- (4-fluorophenyi)-3-hydron/ethyifibis}-4- one-midin-3-yiphenovyionyi)ghyyi-D-hydre	0.3	
1-(4-fluorphony)-3-(R)-(8-(Main-phony)-2- hydrony-mhythis)-4-(R)-(8-(R)-(M-(N-(N-(N-(N-(N-(N-(N-(N-(N-(N-(N-(N-(N-	0.09	

1. A compound of formula (I):

myl group may be optionally substituted by one or two substitutents rejected from halo, hydroxy, $C_{1,0}$ alkyl or $C_{1,0}$ alkoxy,

 \mathbb{R}^3 is hydrogen, alkyl, hain, $C_{1-\alpha}$ alkowy or $C_{1-\alpha}$ elkyl \mathbb{R} ;

R⁴ is hydrogen, C₁₋₆ alkyl, halo or C₁₋₆ alkony; R⁴ is hydrogen, C₁₋₆ alkyl, or mylC₁₋₆ alkyl;

wherein R³ and R² may form a ring with 2-7 outbox stones and wherein R⁵ and R² may form a ring with 3-6 carbox stones:

or a pharmscemically acceptable saft, solivate, tolvate of such a saft or a prodrug thereof;

whereig:

R¹ is hydrogen, C_{1-a}sikyl, C_{2-a}cycloalkyl or snyl; wherein said C_{1-a}sikyl insy be optionally substituted by one or more hydroxy, amino, guanidiao, earbonoyl, carboxy, C_{1-a}sikoxy, N—(C_{1-a}sikyl)amino, N,N-(C_{1-a}sikyl)amino, C₁-C_a alkylcarboxylamino, C₁-klylS(O)_a wherein a is 0-1. C_{2-b}cycloalkyl or nryl; and wherein any snyl group may be optionally substituted by one or two substitutetts salacind from halo, hydroxy, C_{1-a}sikyl or C_{1-a}sikoxy;

halo, hydroxy, C_{1-c}alkyl or C_{1-c}alkoxy;

R² and R³ are independently hydrogen, a branched or unbranched C_{1-c}alkyl, C_{2-c}cycloulkyl or aryl; wherein said C_{1-c}alkyl may be updocally substituted

with the provise that said compound is not 3-(R)-4-(R)-1-(phonyl)-3-[2-(4-therephonyl)-2-hydroxyeth-yhulphonyl]-4-[4-(N-[N--[(R)-1-(ex-boxy)-2-(hydroxy)-thyl]curbsmoy/mathyl)-tarbamoy/mothoxy)
phonyl]curidin-2-one; or 3-(R)-4-(R)-1-(phonyl)-2-[2-[4-therephonyl]-2-hydroxyethylsulphonyl]-4-[N--((R)-a-(N--[(S)-1-(ex-boxy)-2-(hydroxy)-k-thyl]curbamoy/]-bentyl]curbamoy/]-ethyl]curbamoy/]-bentyl]curbamoy/]-actidin-2-one.

2. A compound of formula (12):

"N,N" ->

by one or more hydroxy, amino, amnidino, cyano, carbamoyi, carboxy, $C_{1,0}$ alkoxy, $C_{1,0}$ alkoxy, (C_1,C_2) Si, $N-(C_{1,0}$ alky)iomino, (AA) $(C_{1,0}$ alky) $(C_{1,0}$ alky)iomino, $(C_{1,0}$ alky)iomi

wherein:

R¹ is hydrogen, C_{1-s}alkyl, C_{2-s}systoalkyl or myl;

wherein said C_{1-s}alkyl may be optionally substituted
by one or more hydroxy, semino, guanidian, olubanoyl, carboxy, C_{1-s}alkoxy, N—(C_{1-s}alkyl)amino,

US 2008/0064676 A1

Mar. 13, 2008

68

missing .

V K

N.N.(C_{1.0}elkyl)₂maino, C₁-C₀ sikylmatomylamino. C_{1.0}elkylS(O)₀ wherein a is 0-2, C_{1.0}cycloolky) or eryl; and wherein any eryl group may be optionally enbuitmed by one or two substituents selected from halo, hydroxy, C_{1,0}alkyl or C₁₋₆alkoxy;

R³ and R⁵ are independently hydrogen, a branched or unbranched C_{1.6}alkyl, C_{2.6}cycloalkyl or aryl; wherein said Ci_alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, syuco, carbamoyi, carboxy, C_{1-d}alkoxy, aryl C_{1-d}alkoxy, (C₁-C₄)₃Si, N=(C_4lly)|amino, NN-(C₁₋₄ally)).

2amino, C₁-(ally)S(O), G₂-cyclosikyi, aryl or aryl C, alkyl5(O), wherein a is 0-2; and wherein any 24 paries aryl group may be optionally substituted by one of two substituents selected from halo, hydroxy, C. dikyl or C. dillowy;

> R3 is hydrogen, alkyl, halo, C, subserv or C, o alkyls---:

R⁴ is hydrogen, C₁₋₂ alkyl, halo or C₁₋₂a9coxy;

R⁶ is hydrogeo, C₁₋₀ alkyl, or saylC₁₋₀ alkyl;

wherein R³ and R² may form a ring with 2-7 carbon stoms and whereig R⁴ and R³ may form a ring with 3-6 carbon

or a pharms conticully acceptable sait, solvate, solvate of such a selt or a prodrug thereof,

with the provise that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxycthylstulphagy()-4-[4-(N-{N--|(R)-1-(carboxy)-2-(hydruxy)ethyl]carbamoylmethyl]ourbamoylmethoxy) phenyl]azzidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyi)-2-bydroxycthylsulphanyl]-4-{4-{N ((R)(K-)N [(B)-1-(=arhoxy)-2-(hydroxy) ethyl]carbamoyi]benzyl)carbamoylmethoxyl phenyl}azetldin-2-onn.

3. A compound according to chim 1, wherein:

R1 is hydrogen or phonyl,

4. A compound according to cistm 1, wherein:

R² is hydrogen, a branched or unbranched C_{1.5}slkyl, Careyelosiky) or aryl; wherein said Carelleyl may be y optionally asbatituted by one or more hydroxy, amino, mylandao,

C1. pallcyl5(Ca) therein a is 0-2, C3_cyclosikyl or sryl: and wherein any anyl group may be optionally substitoted by hydroxy, alkyl, alkoxy or cyano.

5. A compound according to claim 1, wherein:

R³ is hydrogen, C₁-C₂ulkyl, halo or methoxy.

6. A compound seconding to obtin 1, wherein:

R³ is hydrogen, methyl, chlorine, fluorina, C₁₋₄ alkylS , or methoxy.

7. A compound eccording to chim 1, wherein:

R4 is hydrogen or halo.

8. A compound according to claim 1, wherein:

R4 is chlorine or fluoring.

9. A compound according to claim 1, wherein:

R⁶ is hydrogen, C₁₋₆ alkyl, srylC₁₋₆sikyl or R⁶ and R³ form a ring with 3-6 carbon atoms.

10. A compound according to claim 1, wherein:

R is hydrogen.

R2 is a branched or unbranched Chalkyl, optionally substituted by a Chargelosikyl, alleyis..., anyl optionally substituted by hydroxy or cyano, amino, N-(C₁. salkyl)amino, N,N-(C1.4alkyl)2-amino or aryl C1.4 alkylS(O),, wherein s is 0-2;

R" and R" are halo;

Rs is hydrogen or Ci., alkyl; and

Ro is hydrogea.

11. One or more compounds chosen from:

N-{[4-((2R,3R)-1-(4-floorophenyl)-3-{[2-(4-flooropheayl)-2-hydroxyethyl]thio}-4-oxxazanidin-2-yl)phenoxy] acctyi)glycyl-N6-acctyi-D-lysinc;

1-(4-l/borophenyl)-3-(R)-[2-(4-fluorophenyl)-2-hydroxycthy?thio)-4-(R)-{4-[N-{N-[Z-(phenyl)-1-(R)-(carboxy)cthyl]carbamoyimethyl]carbamoyimethoxy] phonyl azetidin-2-me;

N-.[[4-((2ft,3R)-1-(4-Huorophenyl)-3-[[2-(4-Huorophenyl)-2-hydroxyothyljshio}-4-oxoazetidin-2-yl)phenoxyj soctyl)glycyl-D-valine;

N-{|4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyljthio}-4-oxoszetidio-2-yl)phonoxy) acetyi] glycyl-D-tytoxine;

N-{[4-((2R,3R)-]-(4-fluoropheayl)-3-[[2-(4-fluoropheny/13-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phanoxy] scety)]glycy[-D-proline;

N-{[4-((2R,3R)-]-(4-fluorophonyl)-3-{[2-(4-fluorophonyl)-2-hydroxycdryl]thio}-4-exoszetkin-2-yl)phenoxy] acetyl) glycyl-D-lysine;

N-{[4-((2R,3R)-1-(4-floorophenyl)-3-{[2-hydroxy-2-(4methoxypheayl)etityi|thio}-4-consectidia-2-yi)phenoxy| acetyl)glypyl-D-valine.

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydraxyethyl]thlo}-4-oxosymidin-2-yl)phenoxy] negty) glycyl-2-butylion/encine;

N-{[4-((2R,3R)-1-(4-Flacerophenyl)-3-{[2-(4-fluorophenyl)-3nyl)-2-hydroxysshyl]thio}-4-oxozzetidh-2-yl)phenoxy] acetyl}glycyl-5-methyl-L-cymeine;

 $N-\{(4-((2R,3R)-1-(4-chlorophenyl)-3-\{|2-(4-chlorophe$ nyl)-2-hydroxyothyl]thio}-4-oxoszetidin-2-yl)phcnoxy] soctyl) gtycyl-3-cyclobacyl-D-slamine;

N-{|4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluoropheayl)-2-hydroxynthyl]thio}-4-oxoazetidiz-2-yl)phenoxy] acetyl)glycyl-3-cyclobexyl-D-alanine;

N-{[4-((2R_a3R)-)-(4-fluorophenyl)-3-{(2-(4-fluorophenyl)-2-hydraxyethyl ffylg)-4-oxunzetidin-2-yl)phenoxy] acetyl)glycyl-4-methyljcpcinu;

N-{[4-((2K,3R)-1-(4-Photophenyl)-3-([2-(4-fluorophenyl)-2-hydroxycthyl]thio}-4-exceszetidin-2-yl)ph==exy] acqyi}-i,-almyl-D-valine;

rorantit.

methyl teucine

PAGE 4/24 * RCVD AT 7/9/2008 4:18:46 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-4/13 * DNIS:2738300 * CSID: * DURATION (mm-ss):16-32

69

Mar. 13, 2008

N-[[4-((2R,3R)-1-(4-finorophenyl)-3-{[2-hydroxy-2-(4-methylphenyl)ethyl]thio}-4-excezettkin-2-yt)phenoxy} sectyl]glycyl-ID-valine;

N-{[4-((2R,3R)-1-(4-chlorophenyl)-3-{[2-(4-chlorophenyl)-2-hydroxyethyl]thio}-4-oxoazsidin-2-yl)phenoxy] actyl]ghysyl-D-valine;

N-{[4-((2R,3R)-1-(4-chlorophenyl)-3-{(2-(4-chlorophenyl)-2-hydroxyethyl)thio}-4-oxonzenidin-2-yl)phenoxy]
acetyl}glysyl-3-mothyl-D-valine;

N-{[4-((ZR,3R)-1-(4-fluorophenyi)-3-{[2-(4-fluorophe- \nyi)-2-bythoxyethyi)thio}-4-oxonzotidin-2-yi)phecoxy) scetyi}giyeyi-3-(2-naphthyi)-D-alsoine;

N-{[4-((2R,3R)-1-(4-flumophenyl)-3-([2-(4-flumophenyl)-2-hydroxyethyl]thio}-4-oxosoxidin-2-yl)phenoxy)
scryl}glycyl-3-methyl-D-valine;

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-[[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoszetidin-2-yl)phenoxy] scetyl}ghyyl-(3R,4S,5R)-3,4,5,6-tetrahydroxy-D-norleucine;

N-{(4-((2R,3R)-)-(4-Pluorophenyl)-3-{(2-(4-fluorophenyl)-2-lrydroxycthyl]thio}-4-oxoazatidin-2-yl)phenoxyl y x 7 soetyl glycyl-N,2 dimethylateniae;

N-{{-\(28,38,\)-1-{4-Phonopheny\)}-{-(\(\)2\) ydroxy-2-{4-(racthyllhio)pheny\]jethyl}-thio)-4-consectatio-2-v\] phonoxy\secty\)glycyl-3-mothyl-D-valio-veline-

N-{[4-((2R,3R)-1-(4-flumophenyl)-3-{[2-(4-flumophenyl)-2-bydroxyethyl]thio}-4-onomenidin-2-yl)phenoxy]
scetyl}glycyl-S-(4-pothylbenzyl)-D-cysteine;

N-[[4-((2R,3R)-1-(4-fluorophenyl)-1-[[2-(4-fluorophenyl)-2-hydrucyethyl]thio]-4-oxeazetidin-2-yl)phenoxy] seetyl]glycyl-S-(tert-botyl)-D-cysteine; and

N-{|4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoszetidin-2-yl)phenoxy] scetyl}glycyl-b,b-dimethyl-D-phenylalanino.

12. A compound of the formula (XV) or hydrolysable esters or amides thereof:

wherein:

R¹ is hydrogen, C_{1.0}alkyl, C_{2.4}cycloalkyl or aryl; wherein said C_{1.0}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbanocyl, carboxy, C_{1.0}alkyl, N—(C_{1.0}alkyl)amino, NAN (C_{1.0}alkyl)₂amino, C_{1.0}c. alkyloarboxy-

lamino, C_{1-d}alkyIS(O)_a wherein a is 0-2, C_{1-d}syolcolkyl or anyl; and wherein any anyl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-d}alkyl or C_{1-m}alkoxy;

R³ and R³ are independently hydrogen, a branched or unbranched C_{1-c}alkyl, C_{1-c}oycloulkyl or aryl; wherein sold C_{1-c}alkyl may be optionally substituted by one or more hydroxy, amino, guanthino, carbamoyl, carboxy, C_{1-c}alkoxy, aryl C_{1-c}alkoxy, (C₁-C_{1-c}alkyl) amino, C_{1-c}alkylS(O) and C₁₋

R³ is hydrogen, alkyl, halo, C_{1-s}alkowy or C_{1-s} alkylS--:

 \mathbb{R}^4 is hydrogen, C_{1-6} alkyl, halo or C_{1-6} alkyl; \mathbb{R}^4 is hydrogen, C_{1-6} alkyl, or anyl C_{1-6} alkyl; and \mathbb{R}^7 is an hydroxy group; or a C_{1-9} alkoxy group;

wherein R³ and R² may form a ring with 2-7 carbon atoms and wherein R⁶ and R² may form a ring with 3-6 carbon

or a pharmaceurically acceptable salt, solvate, solvate of such a salt or a produce thereof.

with the provise that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-finerophenyl)-2-hydroxyeth-ylsolphenyl]-4-[4-(N-{N--[(R) — 1-(carboxy)-2-(hydroxy)ethyl]

carbamoyimethyl}carbamoyimethoxy)phenyl]
ezetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-(2-(4-(lucrophenyl)-2-hydroxyethylsulphanyl)-4-(4-[N—((R)-o-(N—((S)-1-(carbaxy)-2-(hydroxyethyl)]
earbamoyi|benzyl)carbamoyimethoxy]
phenyl}oretddin-2-one.

13. A method of treating or preventing a hyperlipidemic condition comprising the administration of an effective amount of a compound according to claim 1 to a mammal in hand thereof.

14. A method of trusting or preventing atheresclement comprising the administration of an effective amount of a compound according to claim 1 to a manneral in need thereof.

15. A method for treating or preventing Alzhamers' discuse comprising the administration of an effective amount of a compound according to claim 1 to a mammal in need thereof.

16. A method for treating or preventing a cholesterol associated numer comprising the administration of an officative amount of a compound according to claim 1 to a manufact in need thereof.

17. A pharmaceutical formulation comprising a compound according to their I in ediminators with a pharmaceutically acceptable adjuvent, dilucut and/or carrier.

US 2008/0064676 A1

Mar. 13, 2008

70

A combination of a compound according to formula

wherein:

R¹ is hydrogen. C_{1-s}alkyl C_{3-c}cyclosikyl or aryl; wherein said C_{1-s}alkyl may be optionally substituted by one or more hydroxy, amino, guznidino. carbanyoyl, carboxy, C_{1-s}alkoxy, N—(C_{1-s}alkyl)amino, N.N-(C_{1-s}alkyl)₂amino, C₂-C₃ alkylamoxylamino, C₃-C₄ alkylamoxylamino, C₃-C₄ alkylamoxylamino, C₃-C₄ alkylamoxylamino, C₃-C₄ alkylamoxylamino, C₃-C₄ alkylamoxylamino, C₄-C₄ alkylamoxylaminoxylaminoxylaminoxylaminoxylaminoxylaminoxylamin

halo, hydroxy, C_{1-e}sikyl or Cypikoxy;

R² and R³ are independently hydrogen, a branched or unbranched C_{1-e}sikyl C_{2-e}cyclosikyl or aryl; wherein said C_{1-e}sikyl may be optionally substituted by one or more hydroxy, smino, guanidino, cyano, cartesistyl.

carboxy, C_{1-s}alkoxy, aryl C_{1-s}alkoxy, (C₁-C_n),Si, N--(C_{1-s}alkyl),mnino, N₁N-(C_{1-s}alkyl),mnino, C_{1-s}alkylS(O)_s, C_{2-s}oycloxikyl, aryl or aryl C_{1-s}alkylS (O)_s, wherein a is 0-2; and wherein any styl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-s}alkyl or C_{1-s}alkoxy; R³ is hydrogen, alkyl, halo, C_{1-s}alkoxy or C_{1-s}alkylS—;

R⁴ is thydrogen, C_{1-e}sikyl, halo or C_{1-e}sikony; R⁶ is hydrogen, C_{1-e} alkyl or sryfC_{1-e} alkyl; wherein R⁵ and R² may form a ring with 2-7 carbon atoms and wherein R⁴ and R² may form a ring with 3-6 carbon glome;

or according to formula (12)

JUL-09-2008 15:29

US 2008/0064676 A1

Mar. 13, 2008

71

wherein:

R¹ is hydrogen, C_{1-c}alkyl, C_{2-c}oyoloalkyl or aryl;

wherein said C₁alkyl may be optionally substituted
by one or more hydroxy, amino, guanidino, excham
by one or more hydroxy, amino, guanidino, excham
cyl, carboxy C_{1-c}alkoxy, N- (C_{1-c}alkyl)amino,

(C_{1-c}alkyl)amino, C_{1-c}alkyl)amino,

wherein a is 0·2, C_{2-c}ayelosikyl or aryl; and wherein
any aryl group may be optionally substituted by one
of two substitutents selected from halo, hydroxy,

C_{1-s}alkyl or C_{1-s}alkoxy; R² and R³ are independently hydrogen, a bounched or unbranched C_{1-s}alky)

C₁-syclosikyl or aryl; wherein said C_{1.4}alkyl may be optionally substituted by one or more hydroxy, arthropy, granding, eyeng, carbamoyl, earboxy, C_{1.4}alkoxy, aryl C_{1.5}koxy, (C_{1.5}C_{1.5}Sl, N—(C_{1.4}alkyl)minto, N, (C_{1.5}alkyl)minto, N, (C_{1.5}alkyl)minto, N, (C_{1.5}alkyl)minto, C_{1.5}alkyl)minto, N, or aryl C_{1.5} alkylS(O)₆, wherein a is 0.2; and wherein any gryl group may be optionally substituted by one or two substituents selected from halo, hydroxy.

Calkyl of Chykray;
is hydrogen, alkyl, halo, Chalkosy or Che
alkyl;
is hydrogen, alkyl, halo, Chalkosy or Che

 \mathbb{R}^d is hydrogen, C_{1-d} effect, halo or C_{1-d} effect; \mathbb{R}^d is hydrogen, C_{1-d} affect or enyi C_{1-d} affect

wherein R⁵ and R² may form a ring with 2-7 curbon atoms and wherein R⁴ and R² may form a ring with 3-6 carbon atoms;

with a PPAR alpha and/or gamma agents;

19. A combination of a compound according to familia
(f)

therein:

R' is hydrogen C_{1.0}alkyl, C₂cythoalkyl or anyl;

whencin said C_{1.0}alkyl havy be optionally substituted
by one or more hydroxy, staine, generation, carban-

oyl, carboxy—Contakoxy. N (Contayl) armo, N.N-(Contayl) armon, Contayls (O), wherein is O2. Contayls (O), wherein any anyl group may be optionally substituted by one or two substituents selected from halo, hydroxy, Contayls or Contakyl or Contaky

R² and R⁶ are independently hydrogen, a branched or unbranched C_{1-a}sikyl C_{1-a}sikyl C_{1-a}sikyl or aryl; wherein said C_{1-a}sikyl may be optionally substituted by one or more hydroxy, amino, guantidine, cysgo, cartemoyl, carboxy, C_{1-a}sikosy, styl C_{1-a}sikory, (C_{1-C})₃Si, N·(C_{1-a}sikyl)uminoy Tr.N·(C_{1-a}sikyl)₂amino, C_{1-a}sikyl)₂mino, C_{1-a}sikyl)₂mino, C_{1-a}sikyl)₂mino, C_{1-a}sikylS(O)_a, C_{1-a}sikylSyl, aryl or myl C_{1-a}sikylS (O)_a, wherein a is O-2; and wherein any myl group may be optionally substituted by one or two substitutions effected from halo, bydroxy, C_{1-a}sikyl or C_{1-a}sikoxy; R²· is hydrogen, alkyl, halo, C_{1-a}sikoxy or C_{1-a}sikylS·;

 \mathbb{R}^{4} is hydrogen, C_{1-4} alkyl balo or C_{1-6} alkoxy;

Re is hydrogen, C14 alkyl, or arylC1-8 alkyl;

wherein R³ and R² may form a ring with 2-7 carbon aroms and wherein R⁶ and R² may form a ring with 3-6 carbon atoms; Eamino).

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carbony)

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US 2008/0064676 A1

Mar. 13, 2008

72

or according to formula (12)

wherelin

R¹ is hydrogen, C_{1-s}alkyl, C_{2-c}cyclealkyl or myl; wherein seid C₁-kyl may be optionally substituted by one or more hydroxy, amino, guantian, curbantoyl, earbury C_{1-s}alkoxy. N--(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₁-C₂-klkylcarbonylamino, C₁₋₈lkylS(O)₆ wherein a is 0-2. C₃₋₆cycloslkyl or anyl; and wherein any anyl group may be optionally substituted by one or two substitutes selected from halo, bydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;

unhranched C_{1.c}alkyl C_{2.c}cycloallyl or anyl; wherein said C_{1.c}alkyl may be optionally substituted by one or more bydroxy, tenino, guandino, cyano, cartemoryl, carboxy, C_{1.c}alkoxy, anyl C_{1.c}alkoxy, (C_{1.C})₂Si, N—(C_{1.c}alkyl)amino, N,N-(C_{1.c}alkyl)

2 amino, (C_{1.c}) kylS(O)_s, C_{2.c}oycloalkyl, anyl or anyl C_{1.c} alkylS(O)_s, wherein a is 0.2; and wherein any anyl group may be optionally substituted by one or two substituteds selected from halo, hydroxy, C_{1.c}alkyl or C_{1.c} alkoxy;

R2 and R3 are independently hydrogen, a branched or

R³ is hydrogen, alkyl, halo, C₁₋₄ skoxy or C₁₋₅ alkylS ;

R⁴ is hydrogen, C₁₋₈ alkyl halo or C₁₋₈ alkowy;

R⁶ is hydrogen, C₁₋₆ alkyl or arylC₁₋₆ alkyl; wherein R⁶ and R² may form a ring with 2-7 carbon atoms and wherein R⁶ and R² may form a ring with 3-6 carbon atoms.

with an HMG Co-A reductase Inhibitor.

20. A process for preparing a compound or a pharmacoutically acceptable salt, solvete, solvete of such a salt or a produce thereof comprising: a) reseting a competend of formula (II):

with a compound of formula (III):

b) reacting an acid of formula (TV):

or an activated derivative thereof:

US 2008/0064676 A1

Mar. 13, 2008

73

(Y)

with an amine of formula (V):

c) reacting an acid of formula (VI):

or an activated derivative threatly, with an amine of formule (VII):

d) reducing a compound of formula (VIII):

with a compound of formula (X):

f) reacting a compound of formule (XI):

with a compound of formula (XII):

US 2008/0064676 A1

Mar. 13, 2008

74

g) De-esterifying a compound of formula (XIII)

wherein the group C(O)OR is an error group; and wherein:

R' is hydrogen, C_{1...} alkyl, C_{2...} cycloalkyl or exyl, wherein said C_{1...} alkyl may be optionally substituted by one or more hydroxy, amino, guanidiso, carbanayl, carboxy C_{1...} alkyl, mino, NN-(C_{1...} alkyl) amino, NN-(C_{1...} alkyl) panino, C_{1...} alkyls (O), wherein a is 0-2, C_{3...} cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1...} alkyl or C_{1...} alkoxy;

R² and R² are independently hydrogen, a branched or unbranched C_{1...}alkyl C_{1...}cycloalkyl or aryl; wherein said C_{1...}alkyl may be optionally substituted by one or more hydrogen emino, guanidize, syano, carbanoyl, carbony, C_{1...}lkoxy, aryl C_{1...}alkoxy, (C_{1...}C_{1...})k. N.-(C_{1...}alkyl)₂amino, N.N-(C_{1...}alkyl)₂amino, C_{1...}glkylS(O)_{2...}C_{2...}cycloalkyl aryl or aryl C_{1...}alkylS(O)_{2...}cycloalkyl aryl or aryl group may be optionally substituted by one or two substituted by one or two substituted accorded from halo, bydroxy, C_{1...}alkyl, or C_{1...}alkoxy; R³ is bydrogen, ulkyl, halo, C_{1...}alkoxy or C_{1...}alkylS--; R⁴ is hydrogen. C_{1...}alkyl, halo or C_{1...}alkoxy;

R⁶ is hydrogen, C_{1,0} sikyl or anylC_{1,0} sikyl; wherein R⁵ and R² may form a ring with 2-7 carbon atoms and wherein R⁶ and R² may form a ring with 3-6 carbon atoms; and

L is a displaceable group; and thereafter optionally:

 i) converting a compound of the formula (I) into snother compound of the formula (I);

f) nemoving any protecting groups;

(ii) faming a pharmaconically acceptable salt, solvate, solvate of such a salt or a product or

iv) separating two or more enantiomers.

21. A method of treating or preventing a hyperlipidemic condition comprising the administration of an affective amount of a compound according to claim 12 to a meaning in peed thereof.

22. A method of treating or prevening stheroscierosis comprising the administration of an effective amount of a compound according to claim 12 to a mammal in need thereof.

23. A method for treating or proventing Alzheimers' disease comprising the administration of an effective amount of a compound according to claim 12 to a manual in need thereof.

24. A method for treating or proventing a cholesterol associated rumor comprising the administration of an effective amount of a compound according to claim 12 to a mammal in part thereof.

mammal in need thereof.

25. A pharmaceutical formulation comprising a compress according to claim 12 in admixture with a pharmaceutically acceptable adjuvant, dilucut and/or corrier.

26. A process according to claim 20 wherein L is a

helogen or sulphonylony group.

27. A process according to claim 26 wherein L is a chloro, home, metamental homelony or, tolume-4-sulphonylony.

brome, median-sulphonyloxy or toluene-4-sulphonyloxy group.

28. A process according to claim 20 wherein the C(O)OR, ester group is methoxycarbonyl, ethoxycarbonyl, t-butoxycarbonyl, or boxyloxycarbonyl.

Carry Cira

Preliminary Arrienament.

DOCKET NO.: ASZN0107-100 (101340-1P US)

PATENT

In the Claims:

The current status of all claims is listed below and supercedes all previous lists of claims.

Please amend claims 1-20, and add new claims 21-28 as follows.

1. (currently amended) A compound of formula (I):

wherein:

R¹ is hydrogen, C_{1-c}alkyl, C_{3-c}cycloalkyl or aryl; wherein said C_{1-c}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-c}alkoxy, N-(C_{1-c}alkyl)amino, N,N-(C_{1-c}alkyl)₂amino, C_{1-c}alkylcarbonylamino C_{1-c}alkylS(O)₄ wherein a is 0-2, C_{3-c}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-c}alkyl or C_{1-c}alkoxy;

R² and R⁵ are independently hydrogen, a branched or unbranched C₁₋₆alkyl,

C₃₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more
hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C₁₋₆alkoxy, aryl C₁₋₆alkoxy, (C₁-C₄)₃Si,

N-(C₁₋₆alkyl)amino (N,N)(C₁₋₆alkyl)₂amino, G₁₋₆alkylS(O)₂, C₁₋₆alkylS(O)₃, C₃₋₆cycloalkyl, aryl or
aryl C₁₋₆ alkylS(O)₃, wherein a is 0-2; and wherein any aryl group may be optionally substituted
by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;

R3 is hydrogen, alkyl, halo, C1.6alkoxy or C1.6 alkylS-;

R4 is hydrogen, C1-salkyl, halo or C1-salkoxy;

R⁶ is hydrogen, C₁₋₆ alkyl, or arylC₁₋₆ alkyl;

PATENT

wherein R⁵ and R² may form a ring with 2-7 carbon atoms and wherein R⁶ and R² may form a ring with 3-6 carbon atoms;

or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof:

with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4illusrophenyl)-2-hydroxyethylsulphanyl]-4-[R-(N-[N-1-(carboxy)-2(hydroxy)ethyl]carbamoylmethyl]carbamoylmethoxy)phenyl]azetidin-2-one; or 3-(R)-4-(R)-1(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-[4-[N-((R)-0-(N-[(S)-1-(carboxy)-2-(hydroxy) ethyl]carbamoyl]benzyl)carbamoylmethoxy]phenyl]szetidin-2-one.

2. (currently amended) A compound of formula (I2):

$$R^{3}$$
OH
 R^{2}
 R^{8}
OH
 R^{2}
 R^{8}
 R^{8}
 R^{2}
 R^{8}

wherein:

R¹ is hydrogen, C_{1-c}alkyl, C_{3-c}cycloalkyl or aryl; wherein said C_{1-c}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-c}alkoxy, N-(C_{1-c}alkyl)amino, N,N-(C_{1-c}alkyl)₂amino, G_{1-c}alkylearbenylamino <u>C₁-C₆ alkylcarbonylamino</u>, C_{1-c}alkylS(O), wherein a is 0-2, C_{3-c}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, bydroxy, C_{1-c}alkyl or C_{1-c}alkoxy;

R² and R³ are independently hydrogen, a branched or unbranched C_{1-c}alkyl,

C_{3-c}cycloalkyl or aryl; wherein said C_{1-c}alkyl may be optionally substituted by one or more

hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-c}alkoxy, aryl C_{1-c}alkoxy, (C₁-C₄)₂Si,

N-(C_{1-c}alkyl)amino, N,N-(C_{1-c}alkyl)₂amino, G_{1-c}alkylS(O)₂, C_{1-c}alkylS(O)₂, C_{3-c}cycloalkyl, aryl or

PATENT

aryl C_{1-6} alkylS(O)_a, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6} alkyl or C_{1-6} alkoxy;

R³ is hydrogen, alkyl, halo, C_Lcalkoxy or C_{L6} alkylS-;

R4 is hydrogen, C1-5 alkyl, halo or C1-salkoxy;

R6 is hydrogen, C1.6 alkyl, or arylC1.6 alkyl;

wherein R^3 and R^2 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms;

or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;

with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-[4-(N-{N-[(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoylmethyl]carbamoylmethoxy)phenyl]azetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-{4-[N-((R)-α){N-[(S)-1-(carboxy)-2-(hydroxy) ethyl]carbamoyl}benzyl)carbamoylmethoxy]phenyl]azetidin-2-one.

- (currently amended) A compound according to claim 1 or 2, wherein:
 R¹ is hydrogen or phenyl.
- (currently amended) A compound according to any of the preceding claims claim 1, wherein:

R² is hydrogen, a branched or unbranched C_{1-c}alkyl, C_{3-c}cycloalkyl or aryl; wherein said C_{1-c}alkyl may be optionally substituted by one or more hydroxy, amino, acylamino, C_{1-c}alkylS(O)_a wherein a is 0-2, C_{3-c}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by hydroxy, alkyl, alkoxy or cyano.

5. (currently amended) A compound according to any of the preceding claims claim 1, wherein:

R3 is hydrogen, C1-C2alkyl, halo or methoxy.

PATENT

- (currently amended) A compound according to any of the preceding claims claim 1,
 wherein:
 - R³ is hydrogen, methyl, chlorine, fluorine, C₁₋₆ alkylS-, or methoxy.
- (currently amended) A compound according to any of the proceeding claims claim.
 wherein:
 - R4 is hydrogen or halo,
- 8. (currently amended) A compound according to any of the preceding claims claim 1, wherein:
 - R4 is chlorine or fluorine.
- (currently amended) A compound according to easy of the preceding claims claim 1,
 wherein:
- R^6 is hydrogen, C_{1-6} alkyl, aryl C_{1-6} alkyl or R^6 and R^2 form a ring with 3-6 carbon atoms.
- 10. (currently amended) A compound according to claim 1, wherein:
 - R¹ is hydrogen;
- R² is a branched or unbranched C₁₋₄alkyl, optionally substituted by a C₂₋₆cycloalkyl, alkylS-, aryl optionally substituted by hydroxy or cyano, amino, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino or aryl C₁₋₆ alkylS(O)_a, wherein a is 0-2 0-2;
 - R³ and R⁴ are halo:
 - R⁵ is hydrogen or C₁₋₆ alkyl; and
 - R⁶ is hydrogen.
- 11. (currently amended) One or more compounds chosen from:
- N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyi- N^5 -acetyl-D-lysine;
 - 1-(4-Fluorophenyl)-3-(R)-[2-(4-fluorophenyl)-2-hydroxyethylthio]-4-(R)-[4-[N-[N-[2-

PATENT

- (phenyl)-1-(R)-(carboxy)ethyl]carbamoylmethyl]carbamoylmethoxy]phenyl]szetidin-2-one;
- N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-valine;
- N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-tyrosine;
- N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]scetyl}glycyl-D-proline;
- $N-\{\{4-((2R,3R)-1-(4-fluorophenyl)-3-\{(2-(4-fluorophenyl)-2-hydroxyethyl]thio\}-4-oxoazetidin-2-yl)phenoxy]acetyl\}glycyl-D-lysine;$
- $N-\{[4-((2R,3R)-1-(4-fluorophenyl)-3-\{[2-hydroxy-2-(4-methoxyphenyl)ethyl]thio\}-4-oxoazendin-2-yl)phenoxy]acetyl\}glycyl-D-valine;$
- N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-2-butylnorleucine;
- N-{[4-((2R,3R)-1-(4-Pluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio]-4-oxoazetidin-2-yl)phenoxy]acetyl}giycyl-S-methyl-L-cysteine;
- N-{[4-((2R,3R)-1-(4-chlorophenyl)-3-{[2-(4-chlorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxylacetyl}giycyl-3-cyclohexyl-D-alanine;
- N-{[4-((2R,3R)-1-(4-fluorophenyi)-3-{[2-(4-fluorophenyi)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-3-cyclohexyl-D-alanine;
- N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-4(methylleucine;
- $N-\{\{4-((2R,3R)-1-(4-Fluorophenyl)-3-\{\overline{[2-(4-f]uorophenyl)-2-hydroxyethyl\}thio}\}-4-oxoazetidin-2-yl)phenoxy]acetyl\}-L-alanyl-D-valine;$
- $N-\{[4-((2R,3R)-1-(4-\Pi uorophenyl)-3-\{[2-hydroxy-2-(4-methylphenyl)ethyl]thio}-4-oxoazetidin-2-yl)phenoxylacetyl glycyl-D-valine;$
- N-{[4-((2R,3R)-1-(4-chlorophenyl)-3-{[2-(4-chlorophenyl)-2-hydroxyethyl]thio}-4-oxozetldin-2-yl)phenoxylacetyl)glycyl-D-valine;
- N-{[4-((2R,3R)-1-(4-chlorophenyl)-3-{[2-(4-chlorophenyl)-2-hydroxyethyl]thio}-4-oxozzetidin-2-yl)phenoxy]zeetyl}glycyl-3-methyl-D-valine;
 - N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-

PATENT

oxoazetidin-2-yl)phenoxy[scetyl]glycyl-3-(2-naphthyl)-D-slanine;

 $N-\{[4-((2R,3R)-1-(4-fluorophenyl)-3-\{[2-(4-fluorophenyl)-2-hydroxyethyl]thio\}-4-oxozzetidin-2-yl)phenoxy[ecetyl]glycyl-3-methyl-D-valine;$

 $N-\{[4-((2R,3R)-1-(4-fluorophenyl)-3-\{[2-(4-fluorophenyl)-2-hydroxyethyl]thio\}-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-(3R,4S,5R)-3,4,5,6-tetrahydroxy-D-norleucine. norleucine:$

N-{[4-((2R,3R)-1-(4-Fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetldin-2-yl)phenoxy]acetyl}glycyl-N,2-dimethylalanine dimethylalanine:

N-({4-[(2R,3R)-1-(4-Fluorophenyl)-3-({2-hydroxy-2-[4-(methylthio)phenyl]ethyl)thio)-4-oxoazetldin-2-yl]phenoxy)scetyl)glycyl-3-methyl-D-valine

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}.4-oxoazetidin-2-yl)phenoxy]scetyl}glycyl-S-(4-methylbenzyl)-D-oyutoino cysteine:

 $N-\{[4-((2R,3R)-1-(4-fluorophenyl)-3-\{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxylacetyl}glycyl-<math>S-(tert-butyl)-D-eysteine$ cysteine; and

 $N-\{[4-((2R,3R)-1-(4-fluorophenyl)-3-\{[2-(4-fluorophenyl)-2-hydroxyethyl]thio\}-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-b,b-dimethyl-D-phenylalanine.$

12. (currently amended) A compound of the formula (XV) or hydrolysable esters or amides thereof:

wherein:

valine;

R1 is hydrogen, CL salkyl, C3-scycloalkyl or aryl; wherein said C1-salkyl may be

PATENT

optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy,

C1_calkoxy, N-(C1_calkyl)amino, N,N-(C1_calkyl)2amino, G1-Gcalkylcarbonylamino C1-C2

alkylcarbonylamino, C1-calkylS(O)a wherein a is 0-2. C3-ccycloalkyl or aryl; and wherein any

aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy,

C1-calkyl or C1-calkoxy;

R² and R³ are independently hydrogen, a branched or unbranched C_{1-c}alkyl,
C_{3-c}cycloalkyl or aryl; wherein said C_{1-c}alkyl may be optionally substituted by one or more
hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-c}alkoxy, aryl C_{1-c}alkoxy, (C_{1-C-1}xSi, N(C_{1-c}alkyl)amino, N₁N-(C_{1-c}alkyl)₂amino, C_{1-c}alkylS(O)₂, aryl C_{1-c}alkylS(O)₂, aryl C_{1-c}alkylS(O)₃,
wherein a is 0-2, C_{3-c}cycloalkyl or aryl; and wherein any aryl group may be optionally
substituted by one or two substituents selected from halo, hydroxy, C_{1-c}alkyl or C_{1-c}alkoxy;

R³ is hydrogen, alkyl, halo, C₁₋₆ alkylS-;

R4 is hydrogen, C1-6 alkyl, halo or C1-6alkoxy;

R6 is hydrogen, C14 alkyl, or arylC14 alkyl; and

 R^7 is an hydroxy group or a $C_{1:3}$ alkoxy group; wherein R^5 and R^2 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms;

or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof:

with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-[4-(N-{N-[(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoylmethyl}carbamoylmethoxy)phenyl]azetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-{4-{N-((R)-0-{N-[(S)-1-(carboxy)-2-(hydroxy) ethyl]carbamoyl}benzyl)carbamoylmethoxy)phenyl}azetidin-2-one.

13. (currently amended) A method of treating or preventing a hyperlipidemic condition hyperlipidemic conditions comprising the administration of an effective amount of a compound according to env one of claims 1 to 12 claim 1 to a mammal in need thereof.

PATENT

- 14. (currently amended) A method of treating or preventing atherosclerosis comprising the administration of an effective amount of a compound according to any one of claims 1 to 12 claim 1 to a mammal in need thereof.
- 15. (currently amended) A method for treating or preventing Alzheimers' disease comprising the administration of an effective amount of a compound according to any one of claims 1 to 12 claim 1 to a mammal in need thereof.
- 16. (carrently amended) A method for treating or preventing a cholesterol associated tumor cholesterol associated tumors comprising the administration of an effective amount of a compound according to early one of claims 1 to 12 claim 1 to a mammal in need thereof.
- 17. (currently amended) A pharmaceutical formulation comprising a compound according to any one of claims 1 to 12 claim 1 in admixture with a pharmaceutically acceptable adjuvant, diluent and/or carrier adjuvants, diluents and/or carriers.
- 18. (currently amended) A combination of a compound according to formula (I)

wherein:

R¹ is hydrogen, C_{1-calkyl}, C_{2-ccycloalkyl} or aryl; wherein said C_{1-calkyl} may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-calkyl}amino, M(C_{1-calkyl})amino, MN-(C_{1-calkyl})amino, C₁-C₆ alkylcarbonylamino, C_{1-calkyl}S(O), wherein a is 0-2, C_{2-ccycloalkyl} or aryl; and wherein any aryl group may be

PATENT

optionally substituted by one of two substituents selected from halo, hydroxy, C1_salkyl or C1_salkoxy.

R² and R⁵ are independently hydrogen, a branched or unbranched C_{1-c}alkyl,

C1-ccycloalkyl or aryl; wherein said C_{1-c}alkyl may be optionally substituted by one or more

hydroxy, amino, guanidino.:cvano, carbamoyl, carboxy, C_{1-c}alkoxy, aryl C_{1-c}alkoxy, (C₁-C₄)₃Si,

N-(C_{1-c}alkyl)amino, N.N-(C_{1-c}alkyl)₂amino, C_{1-c}alkylS(O)₆, C_{2-c}cycloalkyl, aryl or aryl C_{1-c}alkylS(O)₆, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or

two substituents selected from halo, hydroxy, C_{1-c}alkyl or C_{1-c}alkoxy;

R³ is hydrogen, alkyl, halo, C₁ calkoxy or C₁ calkylS-;

R4 is hydrogen, C16 alkyl, halo or C1 selkoxy:

R6 is hydrogen. C1-salkyl, or arvlC1-salkyl;

wherein R^5 and R^2 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms;

or according to formula (I2)

(12)

wherein;

R¹ is hydrogen, C_{1-calkyl}, C_{1-caveloalkyl} or aryl; wherein said C_{1-calkyl} may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-calkyl} amino, N, N (C_{1-calkyl}) amino, C₁-C₆ alkylcarbonylamino, C_{1-calkyl} (O), wherein a is 0-2, C_{1-calkyl} or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-calkyl} or C_{1-calkyl}.

R2 and R5 are independently hydrogen, a branched or unbranched C1 calkyl.

PATENT

Cascycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C₁₋₆alkoxy, aryl C₁₋₆alkoxy, (C₁₋₆alkoxy, (C₁₋₆alkoxy, (C₁₋₆alkoxy, aryl or aryl C₁₋₆alkyl)amino, N.N-(C₁₋₆alkyl)amino, C₁₋₆alkyl)amino, C₁₋₆alkyl)amino, C₁₋₆alkyl)amino, C₁₋₆alkyl) aryl or aryl C₁₋₆alkyl) aryl

R' is hydrogen, alkyl, halo, Cicalkoxy or Cicalkyl

R4 is hydrogen, C1-6 alkvl, halo or C1-6 alkoxy.

R⁶ is hydrogen, C₁₋₅ alkyl, or arvlC₁₋₅ alkyl;

wherein R⁵ and R² may form a ring with 2-7 carbon atoms and wherein R⁶ and R² may form a ring with 3-6 carbon atoms;

with a PPAR alpha and/or gamma agonist.

19. (currently amended) A combination of a compound according to formula (I)

wherein:

R¹ is hydrogen, C₁-calkyl C₁-coveloalkyl or arvl; wherein said C₁-calkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C₁-calkoxy, N-(C₁-calkyl)amino, N,N-(C₁-calkyl)amino) C₁-C₂ alkylcarbonylamino, C₁-calkyls(O), wherein a is 0-2, C₃-cycloalkyl or arvl; and wherein any arvl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁-calkyl or C₁-calkoxy;

R² and R⁵ are independently hydrogen, a branched or unbranched C_{1-c}alkyl.

C_{2-c}cycloalkyl or aryl: wherein said C_{1-c}alkyl may be optionally substituted by one or more

PATENT

hydroxy, amino, guanidino, evano, carbamoy), carboxy, C₁-calkoxy, ard C₁-calkoxy, (C₁-C₄)₃Si.

N-(C₁-calkyl)amino, N.N-(C₁-calkyl)amino, C₁-calkylS(O)₁, C₂-cevoloalkyl-aryl or aryl C₁₋₆

alkylS(O)₁, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or
two substitutents selected from halo, hydroxy, C₁-calkyl or C₁-calkoxy;

R3 is hydrogen, alkyl, halo, C talkoxy or Cta alkylS-;

R4 is hydrogen, C16 alkyl, halo of C16 alkoxy;

R6 is hydrogen, C1-6 alkyl, or arviC1-6 alkyl;

wherein R^5 and R^2 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms;

or according to formula (12)

wherein:

R¹ is hydrogen, C₁₋₆alkyl, C₂₋₆cycloalkyl or aryl; wherein sald C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbantovi, carboxy.

C₁₋₆alkoxy, N-(C₁₋₆alkyl)amino, N.N-(C₁₋₆alkyl)amino, C_{1-C}alkylcarbonylamino,

C₁₋₆alkylS(O), wherein a is 0-2, C₁₋₆cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;

R² and R³ are independently hydrogen, a branched or unbranched C_{1-salkyl},

C_{2-c}cyclosikyl or aryl; wherein said C_{1-salkyl} may be optionally substituted by one or more

hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-salkoxy}, aryl C_{1-salkoxy}, (C₁-C₄)-Si,

N-(C_{1-salkyl}) amino, N.N-(C_{1-salkyl}) amino C_{1-salkyl}S(O), C_{2-scyclosikyl} aryl or aryl C_{1-salkyl}s(O), wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or

PATENT

two substituents selected from halo, hydroxy, C1 calkyl or C1 calkoxy;

R³ is hydrogen, alkyl, halo, C₁₋₆alkoxy or C₁₋₆ alkyls-;

R4 is hydrogen, C14 alkvi, halo or C1 calkexy;

R⁶ is hydrogen, C_{1.6} alkyl, or arylC_{1.6} alkyl:

wherein R⁵ and R² may form a ring with 2-7 carbon atoms and wherein R⁶ and R² may form a ring with 3-6 carbon atoms:

with an HMG Co-A reductase inhibitor.

20. (currently amended) A process for preparing a compound of formula (I) or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof which process (wherein variable groups are, unless otherwise specified, as defined in formula (I)) comprises of comprising:

Process 1) a) reacting a compound of formula (II):

with a compound of formula (III):

wherein L is a displaceable group;

Process 2) b) reacting an acid of formula (IV):

PATENT

or an activated derivative thereof; with an amine of formula (V):

Process 3): c) reacting an acid of formula (VI):

or an activated derivative thereof, with an amine of formula (VII):

PATENT

DOCKET NO.: ASZN0107-100 (101340-1P US)

Process 4): d) reducing a compound of formula (VIII):

Process 5): e) reacting a compound of formula (DC):

with a compound of formula (X):

wherein L is a displaceable group;

Process 6): 1) reacting a compound of formula (XI):